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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,093	11/01/1999	PETER RICHARD REEVES	23541-01	6333

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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/423,093	REEVES ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *85-106* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *85-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 85-106 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

3. For convenience, claims 85, 89, 93, and 97, the only independent claims, are reproduced below.

Claim 85. (Previously Presented) A method of testing a sample for the presence of *E. coli* expressing the bacterial polysaccharide O-antigen serotype 0111, the method comprising the steps of:

(a) providing genomic DNA of a sample to be tested;

(b) providing at least one oligonucleotide molecule, wherein said oligonucleotide molecule is at least about 10 nucleotides in length, and hybridizes using high stringent wash conditions to a nucleic acid sequence selected from the group consisting of:

wbdH (nucleotide positions 739 to 1932 of SEQ ID NO: 1);

wzx (nucleotide positions 8646 to 9911 of SEQ ID NO: 1);

wzy (nucleotide positions 9901 to 10953 of SEQ ID NO: 1); and

wbdM (nucleotide positions 11821 to 12945 of SEQ ID NO: 1),

wherein said high stringent wash conditions consists of 3 x 5 min washes in 2 x SSC and 0.1% SDS at room temperature, a 1 hr wash in

1 x SSC and 0.1% SDS at 58°C and 15 min wash in 0.1 x SSC and 0.1% SDS at 58°C;

(c) contacting said genomic DNA with said at least one oligonucleotide molecule to permit said oligonucleotide molecule to hybridize under said high strigent wash conditions to said nucleic acid sequence when present in said genomic DNA; and

(d) detecting any hybridized oligonucleotide molecules, wherein detection of said hybridized oligonucleotide molecules indicates the presence of said *E. coli* in said sample.

Claim 89. (Previously Presented) A method of testing a sample for the presence of *E. coli* expressing the bacterial polysaccharide O-antigen serotype 0157, the method comprising the steps of:

(a) providing genomic DNA of a sample to be tested;

(b) providing at least one oligonucleotide molecule, wherein said oligonucleotide molecule is at least about 10 nucleotides in length and hybridizes using high stringent wash conditions to a nucleic acid sequence selected from the group consisting of:

wbdN (nucleotide position 79 to 861 of SEQ ID NO: 2);

wbdO (nucleotide positions 2011 to 2757 of SEQ ID NO: 2);

wbdP (nucleotide positions 5365 to 6471 of SEQ ID NO: 2);

wbdR (nucleotide positions 13156 to 13821 of SEQ ID NO: 2);

wzx (nucleotide positions 2744 to 3109 of SEQ ID NO: 2); and

wzy (nucleotide positions 858 to 2042 of SEQ ID NO: 2),

wherein said high stringent wash conditions consists of 3 x 5 min washes in 2 x SSC and 0.1% SDS at room temperature, a 1 hr wash in 1 x SSC and 0.1% SDS at 58°C and 15 min wash in 0.1 x SSC and 0.1% SDS at 58°C;

(c) contacting said genomic DNA with said at least one oligonucleotide molecule to permit said oligonucleotide molecule to hybridize under said high strigent wash conditions to said nucleic acid sequence when present in said genomic DNA; and

(d) detecting any specifically hybridized oligonucleotide molecules, wherein detection of said hybridized oligonucleotide molecules indicates the presence of said *E. coli* in said sample.

Claim 93. (Previously Presented) A method of testing a sample for the presence of *S. enterica* expressing the bacterial polysaccharide O-antigen serotype C2, the method comprising the steps of:

(a) providing genomic DNA of a sample to be tested;

(b) providing at least one oligonucleotide molecule, wherein said oligonucleotide molecule is at least about 10 nucleotides in length and hybridizes using high stringent wash conditions to a nucleic acid sequence selected from the group consisting of:

wbaR (nucleotide positions at 2352 to 3314 of SEQ ID NO: 3);

wbaL (nucleotide positions 3361 to 3875 of SEQ ID NO: 3);

wbaQ (nucleotide positions 3977 to 5020 of SEQ ID NO: 3);

wbaW (nucleotide positions 6313 to 7323 of SEQ ID NO: 3);

wbaZ (nucleotide positions 7310 to 8467 of SEQ ID NO: 3);

wzx (nucleotide positions 1019 to 2359 of SEQ ID NO: 3); and

wzy (nucleotide positions 5114 to 6313 of SEQ ID NO: 3),

wherein said high stringent wash conditions consists of 3 x 5 min washes in 2 x SSC and 0.1% SDS at room temperature, a 1 hr wash in 1 x SSC and 0.1% SDS at 58°C and 15 min wash in 0.1 x SSC and 0.1% SDS at 58°C;

(c) contacting said genomic DNA with said at least one oligonucleotide molecule to permit said oligonucleotide molecule to hybridize under said high strigent wash conditions to said nucleic acid sequence when present in said genomic DNA; and

(d) detecting any specifically hybridized oligonucleotide molecules, wherein detection of said hybridized oligonucleotide molecules indicates the presence of said *S. enteria* in said sample.

Claim 97. (Previously Presented) A method of testing a sample for the presence of *S. enterica* expressing the bacterial polysaccharide O-antigen serotype B, the method comprising the steps:

(a) providing genomic DNA of a sample to be tested;

(b) providing at least one oligonucleotide molecule, wherein said oligonucleotide molecule is at least about 10 nucleotides in length and hybridizes using high stringent wash conditions to a nucleic acid sequence selected from the group consisting of:

(a) providing genomic DNA of a sample to be tested;

(b) providing at least one oligonucleotide molecule, wherein said oligonucleotide molecule is at least about 10 nucleotides in length and hybridizes using high stringent wash conditions to a nucleic acid sequence selected from the group consisting of:

wzx (nucleotide positions 12762 to 14054 of SEQ ID NO: 4); and

wbaV (nucleotide positions 14059 to 15060 of SEQ ID NO: 4),

wherein said high stringent wash conditions consists of 3 x 5 min washes in 2 x SSC and 0.1% SDS at room temperature, a 1 hr wash in 1 x SSC and 0.1% SDS at 58°C and 15 min wash in 0.1 x SSC and 0.1% SDS at 58°C;

(c) contacting said genomic DNA with said at least one oligonucleotide molecule to permit said oligonucleotide molecule to hybridize under said high strigent wash conditions to said nucleic acid sequence when present in said genomic DNA; and

> (d) detecting any specifically hybridized oligonucleotide molecules, wherein detection of said hybridized oligonucleotide molecules indicates the presence of said *S. enteria* in said samples.

4. For purposes of examination, claims 85, 89, 93, and 97 have been interpreted as encompassing the use of oligonucleotides (be they primers or probes) of virtually any length. Support for such an interpretation is based on each of the above-reproduced claims stipulating that the oligonucleotide be "at least about 10 nucleotide in length." A review of the disclosure fails to locate support for this breadth of scope within the four corners of the originally filed application. Page 10, lines 9-11, of the specification provides support for using probes, however, the range is closed. For convenience, the relevant part of page 10 is reproduced below.

> The nucleic acids of the invention may be variable in length. In one embodiment they are from about 10 to about 20 nucleotides in length.

It is noted that the cited passage states that this is but "one embodiment." A review of the disclosure, however, fails to locate an adequate written description of any alternative embodiment. Accordingly, the specification has been found to provide an adequate written description of but a single embodiment for the range of oligonucleotides to be used in the claimed method. Therefore, claims 85, 89, 93, and 97 contain new matter. Claims 86-88, 90-92, 94-96, and 98-106, which depend therefrom, fail to overcome this issue and are similarly rejected.

Response to argument

5. At pages 13 of the response of 16 January 2004 applicant presents argument for the withdrawal of the rejection of claims under 35 USC 112, first paragraph, which for convenience, is reproduced below.

> There is no unpredictable nature with respect to the size of the oligonucleotide of the present invention, as it is well-known in the art that probes can be greater than 20 nucleotides. Further, the upper limit of the size of the probe is not relevant to distinguishing over the prior art, i.e., such is not a critical limitation or a critical term.
>
> The specification, at page 5, teaches that the nucleic acids may be variable in length, and that in one embodiment, they are from about 10 to about 20 nucleotides in length. Thus, the range of "about 10 to about 20" is merely an example of one embodiment.
>
> Clearly, the examples in the present application (see also, e.g., Claim 88) teach that the oligonucleotides can be 10 or greater nucleotides in length, and can be greater than 20 nucleotides (e.g., positions 11821-11844 of SEQ ID NO:1 (i.e., 24 amino acids) and positions 12945-12924 of SEQ ID NO:1 (i.e., 22 amino acids)).

6. The aspect of the use of larger probes being predictable is not dispositive of the rejection of claims under 35 USC 112, first paragraph. While larger and smaller probes may be used in the art, obviousness of alternative embodiments cannot be relied upon to satisfy embodiments now claimed but not disclosed in the original application. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

7. As seen above, applicant directs attention to claim 88 as providing support for the breadth of the claim. While one can rely upon original claims for support for embodiments not recited in the specification, such is not available here to applicant as claim 88 is not an original claim. To that end, it is noted that the instant application was filed on November 1, 1999 with claims 1-42. Claims 85-106 were not added until the amendment of June 21, 2002.

8. At page 14, bridging to page 15 of the disclosure, applicant presents argument for the withdrawal of the rejection as it pertains to the rejection of claim 101.

> Applicants respectfully submit that the sequences of oligonucleotide molecules which hybridize to the "sugar-pathway genes specific to the bacterial strains to be detected" were well-known to one skilled in the art, and/or ones skilled in the art would have been able to identify oligonucleotide molecules capable of hybridizing thereto without undue experimentation (see the last paragraph at page 6 of the present specification).

Applicant also directs attention to documents provided in a response of 23 December 2002. In particular part, applicant asserts:

> sugar biosynthetic pathways. These citations show that sugar-pathway genes were well-known in the art, and formed part of the common general knowledge. As a result, one skilled in the art would have been able to use her common general knowledge and routine techniques available in the art to produce oligonucleotide molecules capable of hybridizing to such genes.

9. The argument of applicant has been fully considered and has not been found persuasive. The claims currently before the office are not drawn to a method of making probes. If such were the case, applicant's argument could be found more persuasive. As evidenced above, the current set of claims are drawn to a method whereby one is to use such starting materials. Clearly, probes/primers encompassed by the claimed method fairly encompass any and all strains of any and all species of bacteria. The only thing that limits the bacterial strain is that it be one that the routineer want to detect. Such breadth of scope clearly encompasses organisms that are to be discovered in the future. The specification has not been found to provide an adequate written description of these essential starting materials where the bacterial strain is one known at the time of filing. And clearly, applicant has not provided an adequate written description of that which ahs yet to be discovered.

10. While applicant asserts that the production of probes is within the level of skill in the art, the claims are not, in this instance, rejected over enablement requirements of 35 USC 112, first paragraph. Rather, the claims are rejected as not being adequately supported by the written description of the specification when as here the claimed method requires the use of certain essential starting materials yet the specification does not provide an adequate written description of such. And as seen above, obviousness cannot be relied upon to satisfy the written description requirement.

11. For the above reasons, and in the absence of convincing evidence to the contrary, the rejection of claims 85-106 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 85-106 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,652,102 (Fratamico et al., in view of Liu et al. (*Journal of Bacteriology*, Vol. 178, No. 7, pages 21-2-2107), and US Patent 5,474,796 (Brennan).

16. Fratamico et al., disclose a method whereby nucleic acids from various bacterial strains are amplified via PCR and are subsequently detected. Table 1 and column 5 teach explicitly of detecting nucleic acid sequences derived from *E. coli* serotype 0111.

17. Fratamico et al., does not identify "sugar pathway genes" such as *wzx*.

18. Liu et al., page 2102, right column, teaches that the sugar pathway genes of bacteria that exhibit the O antigens is of significant interest, that that the O-antigen gene clusters of several *E. coli* serovar, including O111, have been sequenced and studied.

19. Liu et al, teach explicitly of gene *wzx* as having been studied.

20. Brennan et al., discloses an array of nucleic acids. As seen in column 9, the array comprises all possible oligonucleotides that are 10 nucleotides in length. Consequently, Brennan discloses every 10-mer probe and primer encompassed by applicant's method. Further, Brennan discloses every gene identified in the claims, including those sequences that hybridize under the specified conditions.

21. It would have been obvious to one of ordinary skill in the art to have modified the procedure of Fratamico et al., such that samples could be tested for the presence of *E. coli* expressing the bacterial polysaccharide O-antigen serotype 0111 as the prior art clearly teaches that such nucleic acids had been not only isolated and characterized (Liu et al.), but that probes and primers for doing such existed in the prior art (Brennan). In view of the explicit motivation found in the art to detect such sugar pathway genes (Liu et al.), and the ability of a routineer in the art to make and use any probe or primer that binds to any sequence of interest, the ordinary artisan would have been amply motivated and would have had a reasonable expectation of success. Therefore, and in the absence of convincing evidence to the contrary, claims 85-106 are

rejected under 35 USC 103(a) as being unpatentable over US Patent 5,652,102 (Fratamico et al., in view of Liu et al. (*Journal of Bacteriology*, Vol. 178, No. 7, pages 21-2-2107), and US Patent 5,474,796 (Brennan).

Conclusion

22. Rejections and/or objections found in the preceding Office action and not repeated hereinabove have been withdrawn.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

24. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

25. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
19 May 2004